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USE OF CANNABIDIOL (CBD) IN GENERALIZED ANXIETY DISORDER: CURRENT EVIDENCE AND THERAPEUTIC PERSPECTIVES

USO DE CANABIDIOL (CBD) EM TRANSTORNOS DE ANSIEDADE GENERALIZADA: EVIDÊNCIAS ATUAIS E PERSPECTIVAS TERAPÊUTICAS

USO DE CANNABIDIOL (CBD) EN TRASTORNOS DE ANSIEDAD GENERALIZADA: EVIDENCIA ACTUAL Y PERSPECTIVAS TERAPÉUTICAS

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Bianca Suellen Ferreira[1], Mayara Cardoso[2], Wanderson Carlos Santos Agra[3], Bruno Henrique Nakagawa[4], Pabllo Adelino Estevam Barbosa[5], Celso Gabriel Donati de Mendonça Duarte[6], João Gonçalves Simões Filho[7], Brenda Maria Leite Ferreira[8], Daniel Gomes Fialho[9], Mariáh França Guimarães Meirelles de Paula[10], Harrison Oliveira Santiago[11], Thays Almeida de Oliveira[12], João Eugênio Henrique Heidemann e Silva[13], Guilherme Ângelo Faria Rickli[14], Valéria Caprioli Breda[15], Ana Cláudia Queiroz Mota Simas[16], Valéria Goulart Viana[17], Anésia Bezerra da Fonsêca[18], Júlio Cézar Reis Protásio[19], Geovani Teixeira Pinto[20], Gabriel Alves Pereira Isac[21]

ABSTRACT

This study aims to review the current scientific evidence regarding the use of *cannabidiol* (CBD) in the treatment of Generalized Anxiety Disorder (GAD). CBD, one of the main phytocannabinoids derived from *Cannabis sativa*, exhibits a consistent anxiolytic potential without inducing significant psychoactive effects, distinguishing it from tetrahydrocannabinol

[1] Graduated in Medicine. Universidade do Vale do Sapucaí (UNIVAS). E-mail: bi.suellen@gmail.com
[2] Graduated in Medicine. Universidad Privada del Este (UPE). E-mail: mayaracds1809@gmail.com
[3] Doctor. Faculdade de Medicina Estácio de Juazeiro do Norte . E-mail: wandersoneq@gmail.com
[4] Doctor. Centro Universitário de Jaguariúna (UNIFAJ). E-mail: bruno.nakagawa02@gmail.com
[5] General Practitioner. Universidade Nilton Lins. E-mail: pabllоestevam@gmail.com
[6] Doctor. Universidade São Judas Tadeu. E-mail: celsodonati@hotmail.com
[7] Doctor. Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA).
E-mail: joaogonsf@outlook.com
[8] General Practitioner. Universidade Federal do Triângulo Mineiro (UFTM).
E-mail: brendamarialeite@hotmail.com
[9] Psychiatrist, Specialist in Emergency Medicine and Intensive Care. Universidade de Mogi das Cruzes.
E-mail: danfialho@hotmail.com
[10] Doctor (Specializing in Geriatrics).Universidade Iguaçu, Campus V. E-mail: mariahfranca96@uol.com.br
[11] Doctor. Universidade Estadual de Santa Cruz (UESC). E-mail: harrison_oliveira@hotmail.com
[12] Doctor. Centro Universitário (CEUNI FAMETRO). E-mail: tha.ys@hotmail.com
[13] Specialist in Family and Community Medicine; Specialization in Psychiatry. Instituto Abuchaim.
E-mail: joaoeugenio.hhs@hotmail.com
[14] Undergraduate in Medicine. Universidade Estadual de Ponta Grossa (UEPG). E-mail: guifrickli@gmail.com
[15] Doctor. Faculdade de Medicina de Petrópolis (FMP). E-mail: valeriacaprioli@hotmail.com
[16] Doctor. Centro Universitário de Volta Redonda (UNIFOA). E-mail: ana.medicadefamilia@gmail.com
[17] Doctor. Faculdade de Medicina de Itajubá (MG). E-mail: dravaleriagoulart@yahoo.com.br
[18] Doctor. Faculdade de Ciências Médicas da Universidade de Pernambuco.
E-mail: anesiafonseca@gmail.com
[19] Doctor. Universidade Católica de Brasília (UCB). E-mail: julio.protasio@icloud.com
[20] Undergraduate in Medicine. Centro Universitário de Belo Horizonte (UNI-BH).
E-mail: geovanitp@hotmail.com
[21] Doctor. Centro Universitário do Cerrado (UNICERRADO). E-mail: gy1el7788@gmail.com

(THC). Preclinical and clinical evidence indicates that CBD modulates the endocannabinoid system and serotonergic receptors, promoting anxiety reduction in both experimental contexts and clinical practice. Although the results are promising, important methodological limitations remain, including small sample sizes, heterogeneous protocols, and the lack of standardized dosages. Current findings suggest that CBD may represent a safe and effective therapeutic alternative, particularly for patients with inadequate response or intolerance to conventional treatments. However, further high-quality randomized clinical trials are needed to strengthen the scientific evidence and support the development of clear clinical guidelines for the rational use of CBD in the management of anxiety.

Keywords: Cannabidiol. Generalized Anxiety Disorder. Mental Health. Medicinal Therapy. *Cannabis sativa*.

RESUMO

O presente estudo tem como objetivo revisar as evidências científicas atuais acerca do uso do *canabidiol* (CBD) no tratamento do Transtorno de Ansiedade Generalizada (TAG). O CBD, um dos principais fitocanabinoides da *Cannabis sativa*, apresenta potencial ansiolítico consistente sem induzir efeitos psicoativos relevantes, diferenciando-se do tetrahidrocanabinol (THC). Evidências pré-clínicas e clínicas indicam que o composto atua modulando o sistema endocanabinoide e os receptores serotoninérgicos, promovendo redução da ansiedade em diferentes contextos experimentais e na prática clínica. Embora os resultados sejam promissores, persistem limitações metodológicas, como o reduzido tamanho amostral, a heterogeneidade dos protocolos e a ausência de padronização de dosagens. Os achados disponíveis sugerem que o CBD pode representar uma alternativa terapêutica segura e eficaz, sobretudo em pacientes com resposta insuficiente ou intolerância aos tratamentos convencionais. Entretanto, reforça-se a necessidade de ensaios clínicos adicionais, de maior rigor metodológico, para consolidar a evidência científica e subsidiar a elaboração de diretrizes clínicas claras para o uso racional do CBD no manejo da ansiedade.

Palavras-chave: *Canabidiol*. Transtorno de Ansiedade Generalizada. Saúde Mental. Terapia Medicinal. *Cannabis sativa*.

RESUMEN

Este estudio tiene como objetivo revisar la evidencia científica actual sobre el uso del *cannabidiol* (CBD) en el tratamiento del Trastorno de Ansiedad Generalizada (TAG). El CBD, uno de los principales fitocannabinoides de *Cannabis sativa*, exhibe un potencial ansiolítico consistente sin inducir efectos psicoactivos significativos, a diferencia del tetrahidrocannabinol (THC). La evidencia preclínica y clínica indica que el compuesto actúa modulando el sistema endocannabinoide y los receptores serotoninérgicos, promoviendo la reducción de la ansiedad en diferentes contextos experimentales y en la práctica clínica. Si bien los resultados son prometedores, persisten limitaciones metodológicas, como el pequeño tamaño muestral, la heterogeneidad de los protocolos y la falta de estandarización de las dosis. Los hallazgos disponibles sugieren que el CBD puede representar una alternativa terapéutica segura y eficaz, especialmente en pacientes con respuesta insuficiente o intolerancia a los tratamientos convencionales. Sin embargo, se refuerza la necesidad de ensayos clínicos adicionales con mayor rigor metodológico para consolidar la evidencia científica y respaldar el desarrollo de guías clínicas claras para el uso racional del CBD en el manejo de la ansiedad.

Palabras clave: *Cannabidiol*. Trastorno de Ansiedad Generalizada. Salud Mental. Terapia Medicinal. *Cannabis sativa*.

1 INTRODUCTION

Anxiety disorders are a heterogeneous set of psychiatric conditions characterized by persistent feelings of fear, apprehension, and excessive worry, often associated with significant physiological and behavioral changes (FROTA et al., 2022; AMERICAN PSYCHIATRIC ASSOCIATION, 2014). Among them, Generalized Anxiety Disorder (GAD) stands out for its high prevalence, chronicity, and substantial impact on quality of life, interfering with social, academic, and professional activities (COSTA et al., 2019; BRAZIL, 2023). It is estimated that, in Brazil, approximately 9.3% of the adult population meets diagnostic criteria for GAD, reinforcing the urgency of effective, safe, and accessible therapeutic strategies (ARAÚJO et al., 2024; BRAZIL, 2024).

Traditionally, the clinical management of GAD involves the use of pharmacological approaches, with emphasis on selective serotonin reuptake inhibitors (SSRIs), benzodiazepines, and, in specific cases, tricyclic antidepressants. Despite being effective, such treatments have relevant limitations, including adverse effects, risk of tolerance and dependence, in addition to heterogeneous therapeutic responses, factors that compromise adherence and long-term success (CARVALHO et al., 2023; CRIPPA; ZUARDI; HALLAK, 2010). In a complementary way, non-pharmacological therapies, such as cognitive-behavioral psychotherapy, demonstrate efficacy, but still face barriers to availability and adherence on a large scale (FROTA et al., 2022).

In this scenario, therapeutic alternatives based on natural compounds, such as cannabidiol (CBD), a non-psychoactive phytocannabinoid derived from *Cannabis sativa*, stand out. Unlike tetrahydrocannabinol (THC), CBD does not induce euphoria or marked cognitive changes, presenting a favorable safety profile and therapeutic potential for several psychiatric disorders, including anxiety, depression, and schizophrenia (HALLAK et al., 2022; ANVISA, 2020). Recent evidence suggests that CBD modulates serotonergic and endocannabinoid neurotransmission, as well as interacting with GABA receptors and oxytocin systems, plausible biological mechanisms to explain its anxiolytic effects (DOS SANTOS et al., 2019; BLOOMFIELD et al., 2022; GUNDUGURTI et al., 2024).

Scientific interest in the use of CBD in anxiety disorders has expanded in recent years, driven by preclinical and clinical evidence demonstrating efficacy in reducing symptoms, without the adverse effects characteristic of traditional drugs (HINDLEY et al., 2022; DENSON et al., 2023). Clinical trials and neuroimaging studies indicate that CBD can reduce the hyperactivity of the amygdala, a central structure in the processing of fear, in addition to

improving emotional regulation, reinforcing its anxiolytic potential (BLOOMFIELD et al., 2022; HALLAK et al., 2022). Systematic reviews corroborate these findings, showing that CBD is well tolerated in different age groups and in patients with psychiatric comorbidities, maintaining a consistent safety profile (BLACK et al., 2019; BILBAO; SPANAGEL, 2022).

In Brazil, the medicinal use of cannabis, including CBD, is regulated by the National Health Surveillance Agency (ANVISA), which recognizes its therapeutic potential for multiple conditions, as long as medical prescription criteria and product quality are observed (ANVISA, 2020). National research reinforces the clinical interest in CBD as an alternative to chemical anxiolytics, highlighting its relevance for public mental health policies and for mitigating the social and economic impact associated with GAD (ARAÚJO et al., 2024; CABRAL et al., 2024). Epidemiological studies also point out that social, economic, and cultural factors contribute to the high prevalence of anxiety disorders, requiring innovative interventions supported by scientific evidence (COSTA et al., 2019; BRAZIL, 2022).

From a pharmacological point of view, CBD has complex properties that involve multiple neurotransmitter systems, highlighting its action on the endocannabinoid system, essential in the regulation of mood, anxiety, and stress (GUNDUGURTI et al., 2024; CAMMÀ et al., 2024). Experimental studies demonstrate dose-dependent anxiolytic effects, with consistent results in animal models subjected to elevated maze tests or acute stress situations (CRIPPA; ZUARDI; HALLAK, 2010; HINDLEY et al., 2022). Such evidence suggests that CBD is a promising alternative, especially in patients with unsatisfactory response or intolerance to conventional treatments.

Additionally, research shows that CBD can act synergistically with other phytocannabinoids and psychotherapeutic therapies, enhancing its clinical effects (CABRAL et al., 2024; CARVALHO et al., 2023). Recent systematic reviews indicate that therapeutic protocols involving CBD can significantly reduce anxiety levels, improve sleep, and increase functionality, without the occurrence of serious adverse events (DENSON et al., 2023; HALLAK et al., 2022). This reinforces its clinical value, especially as an alternative to dependence on benzodiazepines, whose prolonged use is associated with tolerance, excessive sedation, and risk of chemical dependence (CARVALHO et al., 2023).

In the social and economic field, GAD is recognized by the World Health Organization (WHO) and the Pan American Health Organization (PAHO) as one of the main global challenges in mental health (BRASIL, 2022). Chronic anxiety is related to absenteeism, decreased productivity, increased use of health resources, and significant impairments in

quality of life (BRASIL, 2023; FROTA et al., 2022). In this sense, CBD emerges as a potential intervention to reduce such impacts at an individual and collective level.

Despite the promising scenario, the therapeutic use of CBD still faces regulatory, ethical, and scientific barriers, such as the need for standardization of dosages, administration methods, and robust clinical protocols (ANVISA, 2020; HALLAK et al., 2022). Long-term randomized clinical trials are essential to consolidate evidence on efficacy, safety, and mechanisms of action in diverse populations, including children, adolescents, adults, and the elderly (DENSON et al., 2023; GUNDUGURTI et al., 2024). In addition, public perception of the medicinal use of cannabis is still an obstacle, and it is essential to invest in education and awareness strategies aimed at both society and health professionals (ARAÚJO et al., 2024; BRAZIL, 2022).

Therefore, this study proposes to analyze the use of cannabidiol (CBD) in Generalized Anxiety Disorder, focusing on current evidence and future therapeutic perspectives. It seeks to understand the biological mechanisms underlying the anxiolytic effect of CBD, to evaluate its efficacy and safety in preclinical and clinical studies, and to discuss its clinical and social implications in the Brazilian context. The relevance of this study stems not only from the increased prevalence of GAD and its impact on mental health and functionality, but also from the potential of CBD as an innovative, safe, and evidence-based therapeutic alternative (CARVALHO et al., 2023; CABRAL et al., 2024; ANVISA, 2020).

In summary, the introduction of CBD as a therapeutic tool in the management of GAD represents the convergence between scientific advances, clinical needs, and social demands. Recent evidence confirms its potential to reduce anxiety, improve emotional well-being, and promote functionality, consolidating itself as a viable alternative to the limitations of conventional treatments (HINDLEY et al., 2022; BLOOMFIELD et al., 2022; HALLAK et al., 2022). The present review aims to consolidate such evidence, providing subsidies for future research, public policies and clinical practice in the treatment of Generalized Anxiety Disorder.

2 METHODOLOGY

The present research adopts as a methodological approach the **literature review**, configuring itself as a descriptive and analytical study, aimed at systematizing the existing knowledge about the therapeutic use of cannabidiol (CBD) in Generalized Anxiety Disorders (GAD). The bibliographic review is a widely consolidated strategy in scientific production,

allowing the identification, evaluation and synthesis of evidence on a given topic. This approach makes it possible to understand in depth clinical practices, pharmacological mechanisms, and therapeutic developments related to specific interventions (CARVALHO et al., 2023; HALLAK et al., 2022).

The choice of this methodology is justified by the central objective of the study: **to critically analyze the available scientific literature on CBD and its effectiveness in the management of anxiety disorders**. Considering that these disorders are among the main challenges of contemporary mental health, with significant repercussions on the functionality and quality of life of individuals, the literature review is especially appropriate (BRASIL, 2023; COSTA et al., 2019). In addition, the growing interest in alternative therapies and the need to elucidate the safety and efficacy profile of compounds derived from *Cannabis sativa* reinforce the relevance of this methodological approach (ANVISA, 2020; ARAÚJO et al., 2024).

2.1 SOURCE SEARCH AND SELECTION STRATEGY

Data collection was conducted through **a systematic search** in international and national scientific databases, including articles indexed in **PubMed, SciELO, MDPI, BMC Medicine, European Neuropsychopharmacology**, among other journals of relevance to the area. Studies published up to the year **2025** were included, in order to ensure the incorporation of the most recent evidence on the subject (BILBAO; SPANAGEL, 2022; HINDLEY et al., 2022).

For the search strategy, **descriptors compatible with the controlled terminology** of the consulted databases were used, combined with **free keywords**, such as: *"Cannabidiol", "CBD", "Generalized Anxiety Disorder", "Anxiety Disorders", "Cannabinoids*", *"Therapeutic Use"* and *"Psychiatric Disorders"*. The articulation of the terms was carried out using the **Boolean operators "AND" and "OR",** a resource that expanded the scope and increased the precision in the identification of relevant studies (BLACK et al., 2019; CAMMÀ et al., 2024).

The **inclusion** criteria included:

- Original studies and systematic reviews on the therapeutic use of CBD in anxiety disorders, with an emphasis on GAD;
- Research published in Portuguese and English;
- Articles with complete access and available in reliable sources;

- Studies involving human populations, as well as preclinical research relevant to understanding the pharmacological mechanisms of CBD.

Exclusion criteria were established for articles:

- Not related to the central theme of the research;
- Studies of an exclusively opinionated nature without scientific support;
- Outdated publications or with insufficiently described methodology;
- Duplicate revisions or redundant data that compromised the critical synthesis (DENSON et al., 2023; GUNDUGURTI et al., 2024).

2.2 DATA ANALYSIS AND SYNTHESIS PROCEDURES

After the initial selection, the articles were evaluated for **relevance and methodological quality**, considering criteria such as clarity of objectives, adequacy of the study design, description of the sample, methodologies used, and consistency of the results presented (CRIPPA; ZUARDI; HALLAK, 2010; BLOOMFIELD et al., 2022).

Subsequently, the extracted data were **organized into tables and thematic tables**, which made it possible to compare different studies, identify patterns and gaps in the literature, as well as synthesize the available evidence on the efficacy, safety, dosages used, and potential adverse effects of CBD in the treatment of GAD (CARVALHO et al., 2023; HALLAK et al., 2022).

The **critical analysis** also included the discussion of the neurobiological mechanisms underlying the anxiolytic effect of CBD, with emphasis on the modulation of the **endocannabinoid, serotonergic, and oxytocinergic** systems, recognized as fundamental in the regulation of stress and anxiety (DOS SANTOS et al., 2019; GUNDUGURTI et al., 2024). This approach not only described the clinical results, but also allowed us to understand the pharmacological bases that support the use of CBD as a promising therapeutic alternative.

2.3 THEMATIC STRUCTURING OF THE REVIEW

To ensure **coherence and systematization in the presentation of the results**, the literature review was organized into three major thematic axes:

1. **Epidemiology and impact of anxiety disorders** – contemplates the prevalence, associated factors, and repercussions on public health, based on national and international data (BRASIL, 2023; COSTA et al., 2019; FROTA et al., 2022).

2. **Evidence on the use of CBD in GAD** – analysis of clinical trials, preclinical studies, and systematic reviews that investigated the anxiolytic effect of CBD, including comparisons with traditional anxiolytics and evaluation of adverse effects (ARAÚJO et al., 2024; HINDLEY et al., 2022; CABRAL et al., 2024).
3. **Therapeutic perspectives and clinical implications** – discussion of dosage recommendations, dosage forms, limitations of existing studies, and possible future directions for research and clinical practice (ANVISA, 2020; HALLAK et al., 2022; CAMMÀ et al., 2024).

This structure allows the review to be understandable, logical, and capable of systematically presenting the most relevant information for the evaluation of CBD as a therapeutic tool in GAD, ensuring scientific rigor and clinical applicability.

2.4 ETHICAL CONSIDERATIONS AND LIMITATIONS

Although the literature review does not directly involve human subjects, there is a need for **ethical rigor** in the analysis and interpretation of evidence, in order to avoid distortions or undue extrapolations that may compromise the clinical applicability of the findings (ANVISA, 2020; HALLAK et al., 2022).

Among the **expected limitations**, the following stand out: the methodological heterogeneity of the included studies, the differences in the doses of CBD administered, the variations in the anxiety assessment instruments, and the predominance of investigations with small samples or preliminary clinical trials. These constraints will be critically discussed, in order to contextualize the results obtained and indicate directions for future research (BILBAO; SPANAGEL, 2022; BLACK et al., 2019; GOBBI et al., 2019).

2.5 JUSTIFICATION OF THE METHODOLOGY

The choice of the **systematic literature review** as a method is justified by the ability to gather and synthesize scientific evidence from different sources, favoring a critical analysis and the identification of gaps in knowledge about the use of CBD in anxiety disorders. This approach also enables the integration of clinical and preclinical data, providing a solid basis for future recommendations aimed at therapeutic practice and the advancement of scientific research (CARVALHO et al., 2023; DENSON et al., 2023; HALLAK et al., 2022).

By contemplating national and international studies, this methodology contributes to a **contextualized understanding of the Brazilian reality**, considering the current regulatory

aspects, the availability of medical cannabis-based treatments, and the specific needs of the population diagnosed with GAD (ANVISA, 2020; BRAZIL, 2024; CABRAL et al., 2024).

Thus, the methodological approach chosen provides:

- **Scope**: considering different types of studies (clinical trials, systematic reviews and preclinical research);
- **Scientific rigor**: with clear inclusion and exclusion criteria;
- **Clinical relevance**: enabling healthcare professionals to access evidence-based information;
- **Identifying gaps**: which can guide future research on the safe and effective use of CBD in the treatment of anxiety disorders.

In short, the methodology adopted provides a **comprehensive and detailed overview** of the use of cannabidiol (CBD) in Generalized Anxiety Disorder, integrating evidence of an epidemiological, clinical and pharmacological nature. In this way, it is an essential tool for the **theoretical foundation of the study**, in addition to offering relevant subsidies for the formulation of recommendations in clinical practices and for directing future research in the area (HALLAK et al., 2022; GUNDUGURTI et al., 2024; CAMMÀ et al., 2024).

3 RESULTS

Generalized Anxiety Disorder (GAD) is a relevant challenge for global public health, characterized by **excessive worry, constant tension, and persistent physical symptoms**, such as tachycardia, sweating, and sleep disorders (FROTA et al., 2022; BRAZIL, 2024). Epidemiological studies indicate that the prevalence of anxiety in adults in Brazil varies between **9% and 15%,** being influenced by **socioeconomic, genetic, and environmental** factors (COSTA et al., 2019). In this context, the development of **safe and effective therapies** becomes a priority, with **cannabidiol (CBD)** standing out as an emerging alternative of growing scientific interest (ANVISA, 2020; ARAÚJO et al., 2024).

3.1 CLINICAL EVIDENCE OF CBD IN ANXIETY DISORDERS

Cannabidiol (CBD), one of the main phytocannabinoids extracted from *Cannabis sativa*, has demonstrated **consistent anxiolytic effects** in several preclinical models and clinical studies, without inducing the typical psychoactive effects of tetrahydrocannabinol (THC) (CRIPPA; ZUARDI; HALLAK, 2010; GUNDUGURTI et al., 2024). Controlled clinical trials indicate that **acute doses of CBD between 300 and 600 mg** significantly reduce

anxiety levels in stressful situations, such as public speaking tests and simulated social challenges. These effects are comparable to those of conventional anxiolytics, but associated with a **lower incidence of adverse reactions** (BLOOMFIELD et al., 2022; HALLAK et al., 2022).

Recent systematic reviews reinforce these findings, demonstrating that CBD is **effective in different anxiety disorders**, including GAD, social phobia, and post-traumatic stress disorder (HINDLEY et al., 2022; BLACK et al., 2019). Denson et al. (2023) reported that in adolescents and young adults, CBD use not only reduced anxiety symptoms but also promoted **improved emotional functioning and quality of life**, suggesting long-lasting clinical benefits and even **potential neuroprotective effect**.

3.2 NEUROBIOLOGICAL MECHANISMS

The **anxiolytic effect of CBD** is associated with the modulation of **central neurochemical systems**, especially the **endocannabinoid system** and the **serotonergic axis**. Evidence indicates that CBD acts as an **indirect agonist of the 5-HT1A receptor**, promoting anxiolytic and antidepressant effects, in addition to modulating the activity of **CB1 and CB2** receptors, influencing the release of neurotransmitters such as **GABA** and **glutamate** (DOS SANTOS et al., 2019; CAMMÀ et al., 2024). Additionally, its interaction with **the oxytocinergic system** has been suggested as a mechanism for improving social anxiety, favoring **prosocial behaviors** and reducing fear responses (DOS SANTOS et al., 2019).

Functional neuroimaging **studies** corroborate these findings, showing that CBD reduces the **hyperactivity of brain regions** related to anxiety, such as the **amygdala** and **medial prefrontal cortex**, promoting greater balance of neuronal connectivity and emotional regulation (BLOOMFIELD et al., 2022). This **selective neural action** differentiates CBD from traditional anxiolytics, which often induce widespread sedative effects, limiting the functionality of patients.

3.3 COMPARISON WITH CONVENTIONAL THERAPIES

Despite the proven efficacy of **benzodiazepines** and **selective serotonin reuptake inhibitors (SSRIs) in the** management of GAD, these drugs have **significant limitations**, including risk of dependence, occurrence of cognitive side effects, and poor adherence to long-term treatments (ARAÚJO et al., 2024; CABRAL et al., 2024). In this scenario, **cannabidiol (CBD)** emerges as a promising therapeutic alternative, with **a favorable safety**

profile, absence of psychoactive effects, and the possibility of prolonged use without relevant development of tolerance (CARVALHO et al., 2023; HALLAK et al., 2022).

Comparative studies indicate that patients treated with CBD reported **a reduction in anxiety at levels similar to those observed with SSRIs**, but with **a lower incidence of sleepiness, sexual dysfunction, and cognitive changes** (BILBAO; SPANAGEL, 2022; HINDLEY et al., 2022). In addition, the **dosage flexibility** of CBD allows individualized adjustments according to the severity of symptoms, configuring a relevant differential for clinical practice.

3.4 SAFETY AND ADVERSE EFFECTS

The literature demonstrates that **CBD is generally well tolerated**, including at high doses, presenting **mild** and transient adverse events, such as fatigue, gastrointestinal changes, and temporary reduction in appetite (BLACK et al., 2019; GUNDUGURTI et al., 2024). Unlike **tetrahydrocannabinol (THC),** CBD does not induce intoxication, cognitive deficits, or risk of addiction, factors that contribute to its **greater acceptance among patients and health professionals** (CRIPPA; ZUARDI; HALLAK, 2010; HALLAK et al., 2022).

The **National Health Surveillance Agency (ANVISA, 2020)** emphasizes that the use of CBD in mental disorders must be linked to **strict clinical protocols**, including dosage monitoring, monitoring of possible adverse effects, and continuous evaluation of therapeutic efficacy. This recommendation reinforces the relevance of adequate **regulation**, capable of ensuring both **patient safety** and the **standardization of clinical use protocols**.

3.5 LIMITATIONS AND GAPS IN THE EVIDENCE

While the available results are promising, there are still **significant limitations**. Most studies have **small sample sizes**, heterogeneity in administration protocols, and **short follow-up periods**, factors that make it difficult to formulate robust conclusions about the long-term efficacy of CBD (DENSON et al., 2023; CAMMÀ et al., 2024). In addition, most research focuses on **young adults**, which restricts the generalization of findings to pediatric and elderly populations.

Another relevant gap refers to the **lack of standardization** of the CBD products used in the trials, including differences in **concentration**, **cannabinoid spectrum** and **forms of administration**. These variables can significantly influence therapeutic outcomes, making

comparisons between clinical studies difficult (BLOOMFIELD et al., 2022; CARVALHO et al., 2023).

In light of this, future research should prioritize **multicenter, randomized, controlled trials**, conducted with **representative samples** and **prolonged follow-up periods**, in order to consolidate the position of CBD as a **safe, effective, and evidence-based therapeutic alternative** for the management of Generalized Anxiety Disorder.

3.6 THERAPEUTIC PERSPECTIVES

The use of **cannabidiol (CBD)** in the treatment of Generalized Anxiety Disorder (GAD) presents **promising prospects**, especially in the face of the **urgent need for innovation in mental health**, as highlighted by the World Health Organization (WHO) and the Pan American Health Organization (PAHO) (BRASIL, 2022; BRAZIL, 2023). The possibility of integrating CBD into **combined therapeutic protocols**, which combine cognitive-behavioral psychotherapy and conventional pharmacological interventions, configures a **multidimensional** approach to anxiety management.

Recent evidence also suggests the potential of CBD as an **adjuvant in comorbid conditions**, including **depression and chronic pain**, thus broadening its therapeutic spectrum (CABRAL et al., 2024; CARVALHO et al., 2023). The **safety**, **preliminary efficacy**, and **favorable neurobiological profile** cement CBD as a robust candidate for future incorporation into **psychiatric clinical guidelines**.

Additionally, **regulatory evolution**, with emphasis on ANVISA's recognition and the increase in the production of **standardized formulations**, reinforces the practical feasibility of using CBD in clinical routine (ANVISA, 2020). To this end, it is essential to develop **well-designed clinical protocols**, as well as the **continuing education of health professionals** about the rational use of cannabinoids, in order to ensure **safe, consistent, and evidence-based therapeutic results**.

3.7 FINAL CONSIDERATIONS OF THE RESULTS

In summary, the results analyzed show that **cannabidiol (CBD)** has a **consistent anxiolytic effect**, neurobiological mechanisms that are already well characterized, **a favorable safety profile** and **potential for integration** into conventional therapies aimed at the treatment of Generalized Anxiety Disorder (GAD). Current evidence supports the consideration of CBD as a **viable therapeutic alternative**, especially for patients who have

adverse effects or **insufficient response** to traditional anxiolytics. However, the consolidation of this approach still depends on the conduct of **additional clinical trials**, the **standardization of formulations**, and the establishment of **clear therapeutic protocols**.

The future perspective outlines a scenario in which CBD can act not only as a **primary or adjunctive treatment** in anxiety disorders, but also as an integral part of **broader mental health strategies**, aligned with **public policies** and **evidence-based practices**. In this context, its incorporation can contribute significantly to **reducing the social and economic impact of anxiety** on the population (BRASIL, 2022; ANVISA, 2020).

4 DISCUSSION

Generalized Anxiety Disorder (GAD) is among the most prevalent psychiatric conditions worldwide, characterized by excessive worry, muscle tension, irritability, sleep disorders, and difficulty concentrating (AMERICAN PSYCHIATRIC ASSOCIATION, 2014; FROTA et al., 2022). In Brazil, it is estimated that about **9.3% of the adult population** meets diagnostic criteria for anxiety, influenced by **sociocultural, genetic, and environmental** factors (COSTA et al., 2019; BRAZIL, 2023). The impact of GAD transcends the individual sphere, compromising **productivity**, **interpersonal relationships**, and generating greater demand on **health services** (BRASIL, 2022). In this scenario, the search for safe and effective therapeutic alternatives, in addition to conventional anxiolytics, becomes a priority.

In recent years, **cannabidiol (CBD), a** non-psychoactive phytocannabinoid derived from *Cannabis sativa*, has emerged as a therapeutic promise in the management of anxiety disorders. Unlike **tetrahydrocannabinol (THC),** CBD does not induce euphoria or relevant cognitive changes, presenting a favorable safety profile (ANVISA, 2020; CRIPPA; ZUARDI; HALLAK, 2010). Preclinical and clinical evidence suggests that its anxiolytic effect stems from **the modulation of the endocannabinoid system**, with interaction at **serotonin 5-HT1A receptors**, **TRPV1**, and possibly the **oxytocinergic system** (DOS SANTOS et al., 2019; GUNDUGURTI et al., 2024; HALLAK et al., 2022). This **neurochemical multifunctionality** gives CBD the ability to mitigate anxious symptoms without causing the typical adverse effects of benzodiazepines and tricyclic antidepressants, such as excessive sedation, dependence, or cognitive deficit (HINDLEY et al., 2022; ARAÚJO et al., 2024).

Neuroscientific studies show that CBD **reduces the activation of the amygdala and hippocampus** in the face of threatening stimuli, modulating emotional processing and regulating the stress response (BLOOMFIELD et al., 2022). These findings are corroborated

by **systematic reviews**, which identified significant reductions in anxiety levels in patients with GAD, social phobia, and post-traumatic stress disorder, with doses between **300 and 600 mg/day** in controlled clinical protocols (BLACK et al., 2019; HALLAK et al., 2022; GUNDUGURTI et al., 2024). Despite the **methodological heterogeneity**, the results converge to a **consistent, safe and well-tolerated anxiolytic effect**.

From a pharmacological point of view, the action of CBD seems to be **dose-dependent** and influenced by the individual profile of the patient. Moderate doses demonstrate anxiolytic efficacy without causing sedation, while high doses can induce **a biphasic** effect, partially reducing the therapeutic response (BILBAO; SPANAGEL, 2022; CAMMÀ et al., 2024). The **route of administration** also interferes with bioavailability: **oral** formulations have variable absorption and delayed onset, while sublingual formulations ensure more stable pharmacokinetics (CARVALHO et al., 2023). These factors reinforce the need for **individualized protocols**, considering age, body weight, substance history, and psychiatric comorbidities.

In the Brazilian clinical context, **ANVISA** recognizes the safety of CBD in specific conditions, including anxiety disorders, as long as it is prescribed by qualified professionals (ANVISA, 2020). National evidence reports significant improvement in symptoms in patients treated with CBD, without serious adverse effects, suggesting potential as a **complementary alternative** to traditional therapies (ARAÚJO et al., 2024; CABRAL et al., 2024). This makes it especially relevant for individuals with **resistance, intolerance, or contraindications** to conventional treatment.

Still, **methodological limitations** remain. Many clinical studies have **small sample sizes**, **a short follow-up period** , and differences in dosage, formulations, and inclusion criteria (DENSON et al., 2023; HINDLEY et al., 2022). In addition, although the safety profile is favorable, mild adverse events, such as fatigue and gastrointestinal changes, have been reported, especially at **higher doses** (BILBAO; SPANAGEL, 2022; HALLAK et al., 2022). Therefore, clinical use requires **continuous monitoring** and individualized dose adjustment.

Recent research further suggests that CBD may act on **glutamatergic and dopaminergic circuits**, modulating synaptic plasticity and stress response (CAMMÀ et al., 2024; BLOOMFIELD et al., 2022). This neurobiological complexity suggests that CBD not only reduces symptoms, but may **act on the neural regulation underlying anxiety**, opening up new therapeutic perspectives. Pharmacogenomics and **longitudinal follow-up studies**

may identify subgroups of patients with greater responsiveness, expanding the personalization of treatment.

From a socioeconomic and regulatory **point of view**, the incorporation of CBD faces barriers of **access, cost, and social prejudice**. Inclusion in the **SUS** will depend on robust national studies, **cost-effectiveness** analyses, and professional training for rational prescription (ANVISA, 2020; BRAZIL, 2024). Misinformation about medical cannabis can also limit adherence, reinforcing the need for **education of the population and health professionals** (ARAÚJO et al., 2024; CARVALHO et al., 2023).

The integration of CBD should be conceived as a **complementary approach**, associated with **psychotherapy, lifestyle changes, and traditional pharmacotherapy** when necessary (BRASIL, 2024; CABRAL et al., 2024). Integrated management programs can promote **symptom reduction**, **improved quality of life,** and **lower emotional burden**, without compromising patient safety. This model represents an evolution of the biomedical paradigm, with a focus on **patient-centered approaches and personalization of therapy**.

In summary, the national and international literature shows that CBD is a **promising alternative in the** treatment of GAD, with significant efficacy, a favorable safety profile, and plausible neurobiological mechanisms (BLACK et al., 2019; HALLAK et al., 2022; GUNDUGURTI et al., 2024; DENSON et al., 2023). However, the need for **more robust clinical trials**, standardized protocols, and long-term studies is evident. The consolidation of CBD as a therapeutic resource will depend on the integration between **science, public policies and professional education**, ensuring **accessibility, safety and efficacy**.

Therefore, the incorporation of CBD into the therapeutic arsenal of contemporary psychiatry should be seen as an **opportunity for innovation**, combining safety, consistent anxiolytic effect, and potential for personalization. The continuity of **clinical and translational research**, added to the **training of professionals** and the **development of access policies**, is an essential pillar to consolidate CBD as an emerging and transformative strategy in global mental health care.

5 CONCLUSION

The review of the available evidence allows us to affirm that cannabidiol (CBD) presents itself as a promising therapeutic intervention for the management of Generalized Anxiety Disorder (GAD). Its consistent anxiolytic effects, combined with a favorable safety profile and the absence of significant psychoactive properties, differentiate it from traditional

pharmacological approaches and broaden the perspectives of care for patients who do not respond satisfactorily or are intolerant to conventional treatments, such as benzodiazepines and antidepressants.

CBD stands out for its versatility of application, acting both in experimental contexts of stress and in clinical situations of chronic anxiety, with the potential to integrate into multimodal protocols that include psychotherapy and pharmacotherapy. This characteristic paves the way for personalized treatment strategies, capable of considering the patient's individual profile, comorbidities, and symptom severity, in line with the contemporary paradigm of patient-centered psychiatry.

However, despite the encouraging scenario, important challenges remain for its clinical consolidation. The methodological heterogeneity of the studies, the lack of standardization in relation to formulations, dosages, and forms of administration, as well as the limitation of long-term trials, restrict the generalization of the results. Such gaps reinforce the need for multicenter, randomized research with greater methodological rigor, which can provide solid bases for consistent clinical guidelines.

In the Brazilian context, the relevance of CBD goes beyond the clinical sphere, extending to the field of public health. Given the high prevalence of anxiety disorders and the social and economic impact they entail, CBD can contribute to reducing the burden on health services, improving patients' quality of life, and offering more accessible and well-tolerated therapeutic alternatives. For this, it is essential to advance regulation, the production of standardized formulations, and the training of health professionals on the rational use of cannabinoids.

In summary, CBD represents not only an alternative, but an opportunity for innovation in the management of generalized anxiety. Its potential for efficacy, safety, and integration with different therapeutic approaches indicates that, with the maturation of scientific research and the implementation of appropriate public policies, it can be consolidated as a relevant therapeutic resource in modern psychiatry. The future of GAD treatment could be significantly transformed by CBD, as long as it is underpinned by robust evidence, clear regulation, and responsible clinical practices.

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